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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,862	08/19/2003	Michael J. Puglia	017191.0036 (MSA-3459)	5515
7590 Bayer Healthcare LLC 511 Benedict Avenue Tarrytown, NY 10591		08/08/2007	EXAMINER SOOHOO, TONY GLEN	
			ART UNIT 1723	PAPER NUMBER
			MAIL DATE 08/08/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/643,862	Applicant(s) PUGIA ET AL.	
	Examiner Tony G. Soohoo	Art Unit 1723	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-7, 10, 11, 16-26, 29-35 and 37-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-7, 10, 11, 16-26, 29-35 and 37-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention; and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 21-26, 29-35, and 37-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not support the term "predetermined **fixed** liquid volume" (emphasis added, see independent claim 21). Applicant has not address the claim set of claim 21 in the response filed 5/17/2007, page 9.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 25-28, and 29-30, and 36 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Apparatus claims do not claim the actual range or numerical value of the volumes of the "predetermined" volumes of liquid used in the process, however

attempts to provide a structural apparatus limitation of a further chamber in relationship to the volume used during its the device's operation. Apparatus claims 25-28 refer to the volume or depth of fluid (the material to be worked upon by the apparatus) during operation in comparison within the structural chamber to that of the containers, however, since the volume of the first and second liquid amounts dispensed in operation can not been positively determined, the meets and bounds of the relative size of the chambers can not be determined since the size is dependent upon an operational characteristic. "Expressions relating the apparatus to contents thereof during an intended operation are of no significance in determining patentability of the apparatus claim!" *Ex parte Thibault*, 164 USPQ 666, 667 (Bd. App. 1969). "[A]pparatus claims cover what a device *is*, not what a device *does*" (emphasis in original) *Hewlett-Packard v. Bausch & Lomb Inc.* 15 USPQ2d 1525, 1528 (Fed. Cir. 1990).

With regards to claims 29 and 30, the claims point out space in the chamber relative to a flow of fluid during operation of the device and the amount to be provided by the flow. Whereby the flow of fluid is a dependent upon manipulative operation with regards to the amount fed into the chamber, and the claims are directed to an apparatus claim, the space above the level of fluid in the chambers during operation of the fluid flow does not provide a positive patentable structural limitation whereby the level of fluid causing the space is directed to a method of operation and not to a structural feature in an apparatus claim.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 2-4, 6-7, 10-11, 16, 18-26, 29-35, 38, 40, 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kellogg et al 6063589 in view of Koop et al US 6457854 (both previously cited).

The Kellogg et al (Kellogg) reference discloses an apparatus and method including 1st and 2nd fluid wells 601, 601 receivable to accept a 1st predetermined liquid volume in the range of 1 μ L to 150 μ L in each well 601, 601, column 45, line 66-67 through column 46, lines 1-2, whereby the range of the method of operation may choose 1 μ L each thereby providing total mixture of: 1 μ L fluid to be mixed + 1 μ L fluid to be mixed = 2 μ L mixture volume;

or rotation.

As illustrated in FIGS. 15A through 15D, in the use of this platform an equal volume (ranging from 1-150 μ L of fluid)

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3. In of each of the fluids to be mixed was applied to the entry disk ports 601 (FIG. 15A). Fluid entered the each of the metering capillary arrays 602 and stopped at capillary barrier 603.

whereby the liquid volume is dispensed in a dispensing step through capillary passages 602, 602;

into a 1st chamber 605, 610, 606 whereby 605 is an assisting microstructure stepped wall structure to assist in mixing (claims 17, 37), and, as clearly seen provides

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a volume which is much larger than the volume dispensed through the wells and capillary 601, 602 as seen in figure 15d. See Markup on the following page(s).

Also, applicant alleges in the remarks of 5/17/2007 on pages 12-13 that a calculation that of the chamber volumes of 606 is $18.75\ \mu\text{L}$ and 605 is $3\ \mu\text{L}$. The 1st chamber as defined by the Office is 605 ($3\ \mu\text{L}$) plus 606 ($18.75\ \mu\text{L}$) plus 610 (unknown). Addition of the volumes would yield at ($3+18.75+\text{unknown volume}=\text{}$) at least $21.75\ \mu\text{L}$. Thus with regards to the structure in an operation of the total of 1st and 2nd liquid volumes being between $2\ \mu\text{L}$ to $21.75\ \mu\text{L}$, the structure of the 1st chamber would have a volume large than the 1st and 2nd combined liquid volumes.

With regards to the method of operation, when the 1st and 2nd liquid volumes chosen in the method of operation of $1\ \mu\text{L}$ each, the method steps provided by the Kellogg reference involves

a) $1\ \mu\text{L}$ placed into the well 601, the sum (total) of volume processed is $2\ \mu\text{L}$

b) the predetermined volume each is discharged through separate capillary passageways 602,

and discharged into the 1st chamber 605, 610, 606 which has a volume of $18.75\ \mu\text{L}$ which is a volume greater than the sum ($2\ \mu\text{L}$) of the predetermined volumes and would result in free space within the chamber in relation to the level of fluid in the chamber.

FIG. 15A

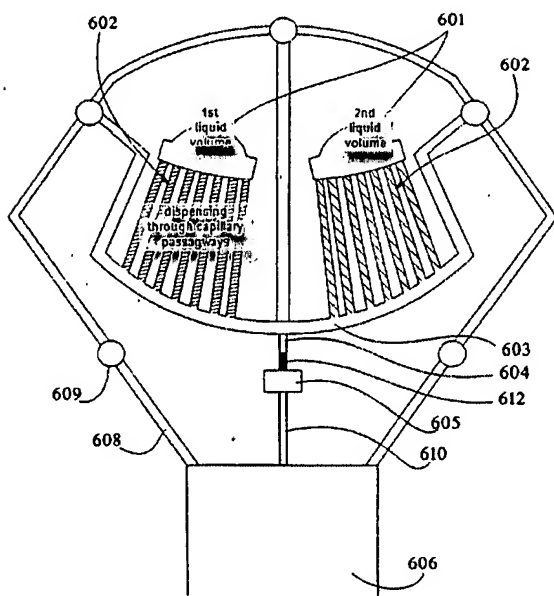


FIG. 15C

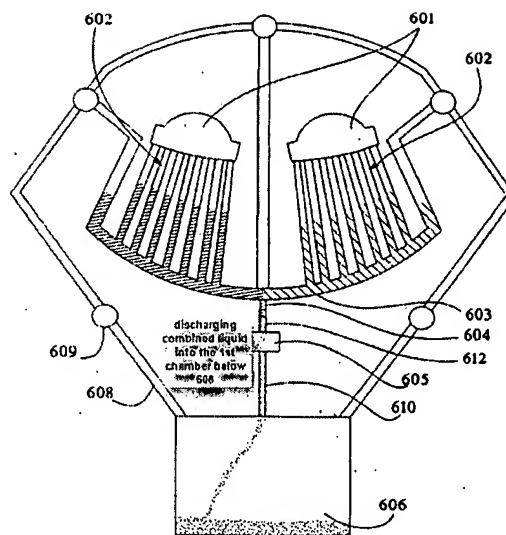
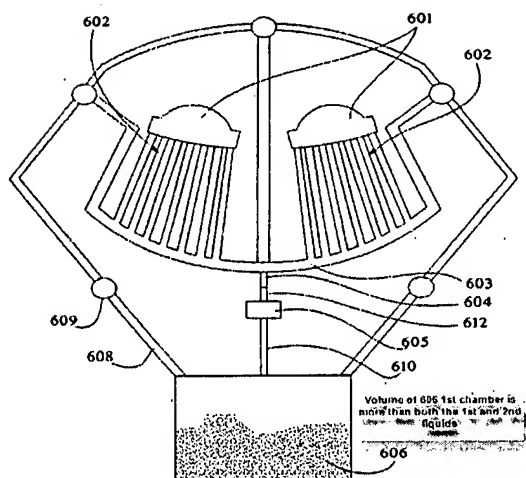


FIG. 15D



The Kellogg (et al) reference discloses all of the recited subject matter as defined within the scope of the claims with the exception of having a further 2nd chamber of the size of the 1st chamber 606, connected to the 1st chamber 606 with at least one capillary passageway and utilizing it to provide further mixing processing of the liquids, or with three connected chambers, or utilizing two or more capillaries between the chambers, or with particular sizing of the capillary or chambers dimensions.

The reference to Koop discloses that one may provide a repeated chamber with at least two connections between the chamber to provide an added mixing effect. The Koop reference shows the state of art that one may provide a chambers which are connected one after another with a connective capillary between the chambers so as to further process the fluid.

The Koop reference discloses an apparatus and method of use for mixing fluids including two inlets for a 1st and 2nd fluid wells to be fed into a 1st chamber at the intersection of 9,10, a second chamber through seventh at the intersection of the sinusoidal loops which are microchannel capillary passageways along the portion 8, see figure 1, which ends at an outlet chamber at 5 for further processing, whereby each loop side may be deemed as separated passageways.

It is also noted that it has been held that mere duplication of the essential working parts of a device involves only routine skill in the art. *St. Regis Paper Co. v. Bemis Co.*, 193 USPQ 8.

It is further noted that Kellogg reference 605, 610, 606 provide a mixing of the two fluids together and desires a mixing of the liquids together.

In light of the showing of the Koop references that one may utilize a use of a device with a repeated connected chambers with plural micro-passageways for added mixing effect, it is deemed that it would have been obvious to one of ordinary skill in the art to duplicate both the mixing chamber and capillary passages in the same manner as shown by the Koop reference so as to provide an added mixing effect upon the fed liquids within the device and method of operation, since it has been held that mere duplication of the essential working parts of a device involves only routine skill in the art. *St. Regis Paper Co. v. Bemis Co.*, 193 USPQ 8.

With regards to having particular volumes, the cross sectional dimension, lengths of the passageways and chambers, a person having ordinary skill in the art in fluid processing would recognize such a size change in geometry would be a direct variable in the production of the amount of fluid which may be processed, and the residence time of processing, accordingly, it is deemed that it would have been obvious to one of ordinary skill in the art to modify the volumes, the cross sectional dimension, lengths of the passageways and chambers so as to optimize the amount of fluid processed and

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the residence time of interaction, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

With regards to the number of passageways between channels, absent any unexpected results with the addition of a 3rd or more channel, it is deemed that it would have been obvious to one of ordinary skill in the art to duplicate at least another channel so that a 3rd sinusoidal pathway is provide to produce additional mixing effect since it has been held that mere duplication of the essential working parts of a device involves only routine skill in the art. St. Regis Paper Co. v. Bemis Co., 193 USPQ 8.

With regards to the amount of level of fluid and velocity of fluid in the method claims, it is commonly known that the level of fluid in a chamber and velocity of fluid flow in a pathway is a direct effective variable in the amount of fluid processed, accordingly absent any unexpected result, it is deemed that it would have been obvious to one of ordinary skill in the art to modify flow velocity and the level of amount of fluid so that the level is of a spacing as recited in the claims so as to optimize the amount fluid that is processed.

With regards to the type of material of the passageways, the use of hydrophilic surfaces in construction of micromixers are old and well known to provide efficient fluid flow, accordingly, it is deemed that it would have been obvious to one of ordinary skill in the art to substitute for the material of the Koop (et al) reference with passages of hydrophilic surfaces so as to better supply a better flow of fluid.

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7. Claims 5, 17, 37, 39, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kellogg et al 6063589 in view of Koop et al US 6457854 as applied to claims 1 and 21 respectively above, and further in view of Jakajima et al 6281254.

The Koop (et al) reference discloses all of the recited subject matter as defined within the scope of the claims with the exception of feeding the fluid in the second chamber in the form of droplets, using ramps or steps to combine the liquids, and structure which prevents premature movement of the fluids.

The Jakajima (et al) reference discloses a mixing channel or chamber 3 having steps or ramp elements 2 which assist in providing a mixing of fluids from the inlet 16 through the inlet chamber 14 to produce droplets at the 2nd side of ramps in the form of droplets, see figure 1; and figure 4, 5, in a controlled movement of the fluids,

In view of the teaching of the Jakajima (et al) reference, it is deemed that it would have been obvious to one of ordinary skill in the art to provide for the chambers of the Koop (et al) reference with ramps which assist in providing a mixing of fluids to produce droplets at the 2nd side of ramps in the form of droplets in a controlled movement of the fluids so as to produce a more effective emulsion of the mixed fluid.

Response to Arguments

8. Applicant's arguments file 17 MAY 2007 have been fully considered but they are not persuasive.

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9. Applicant argues on page 11, that the that the Koop (secondary teaching reference) operates in a continuous mode and therefore not relevant to applicant's invention.

Koop throughout prosecution of this application. The Applicants continue to believe that Koop's device operates in a continuous mixing mode and is therefore not relevant to their microfluidic

device which inherently operates with predetermined liquid volumes, i.e. it is a batch operated device. The Examiner's response to the Applicant's argument makes it clear that, despite the

10. In response, the claims do not recite limitations to exclude a continuous or a batch mode

Since issues of a discrete batch mode has not been claimed in the method step nor such feature is supported in the apparatus claims such as the provision of a structural control system and valves to produce a discrete batch flow, such arguments are immaterial and deemed unpersuasive.

11. Applicant further argues on page 12, that the primary Kellogg reference has a mixing chamber 605 and 606 which is smaller the combined volume of liquids.

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The mixing chamber 605 is clearly smaller than the volume of the combined liquids, as also is the receiving chamber 606. Therefore, Kellogg does not teach essential features of the Applicant's invention, which includes no mixing chamber and uses chambers of larger volume than the liquids being mixed. Fig. 14 is somewhat misleading. As described more definitely at

In response, applicant not considered the amount of fluid to be used in the Kellogg reference, see column 45, line 66-67 through column 46, lines 1-2, whereby the range of the method of operation may chosen as 1 μL each thereby providing total mixture of: 1 μL fluid to be mixed + 1 μL fluid to be mixed = 2 μL mixture volume;

As illustrated in FIGS. 15A through 15D, in the use of this platform an equal volume (ranging from 1-150 μL of fluid)

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3. In of each of the fluids to be mixed was applied to the entry
disk ports 601 (FIG. 15A). Fluid entered the each of the metering
meta- capillary arrays 602 and stopped at capillary barrier 603.

Also in light of applicant's calculation of the volumes of the 1st chamber, 605, 610, 606, it is readily apparent that the chambers are larger then the fluids being mixed, see the discussion in the rejection above.

12. With regards to the Koop reference on page 13, Applicant alleges that the Koop reference is a continuous mixing system and odes not involve predetermined liquid volumes which are combined thus does not the overcome deficiency of Kellogg.

Koop teaches a continuous mixing system which does not involve combining predetermined volumes of liquids by moving them into chambers which have volumes greater than that of the combined liquids. Therefore, Koop does not overcome the deficiency of Kellogg.

13. In response, the Koop reference was utilized as evidence of the common knowledge and a further evidence of a teaching the one may utilize a use of a device with a repeated connected chambers with plural micro-passageways for added mixing effect.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

14. With regards to the Nakajima reference applicant argues:

deficiencies of Kellogg/Koop have already been discussed. Nakajima described an improved device to create emulsions from a dispersed phase and a continuous phase, which emulsions contain microspheres. The Nakajima device employs structures that are far different from those

of the Applicants' device. The Examiner relies on "obvious to one skilled in the art" to combine Nakajima with Koop. However, there is no suggestion anywhere that combining Nakajima with Koop would yield the Applicants' invention. Furthermore, neither Kellogg nor Koop nor the present invention involve forming emulsions. Consequently, Nakajima is non-analogous art.

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1. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that a reference explicitly provide a reason or motivation to combine with another reference.

2. In response to applicant's argument that Nakajima is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the problem at hand is a problem of fluid dynamic feed of material and in particular of feeding the fluid in the second chamber in the form of droplets, using ramps or steps to combine the liquids, and structure which prevents premature movement of the fluids. A person having ordinary skill in the art looks to the Nakajima reference as a manner to solve a problem within a mixing channel, or chamber 3, the feed of material by having steps or ramp elements 2 which assist in providing a mixing of fluids from the inlet 16 through the inlet chamber 14 to produce droplets at the 2nd side of ramps in the form of droplets.

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in a controlled movement of the fluids, thus would find it pertinent to the feed of fluid liquid in the Kellogg device and method.

Conclusion

15. The prior art made of record **previously** made of record and not relied upon is considered pertinent to applicant's disclosure.

Andersson et al 6919058 was previously cited on PTO-892 and shows mixing and dispensing into a cavity 203 of sufficient volume, column 16, line 7.

respectively).

The mixing unit of the present invention is characterized by comprising (a) the microcavity (203) with an outlet opening (223), typically in its lower part; (b) an inlet arrangement (201) linked to the microcavity (203), and (c) a mixing microconduit (202) connected to the outlet opening (223). The microcavity (203) shall have a volume sufficient to contain simultaneously the aliquots to be mixed. The inlet

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of


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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tony G. Soohoo whose telephone number is (571) 272 1147. The examiner can normally be reached on 8AM-5PM, Tue-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David R. Sample can be reached on 571-272-1376. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Tony G Soohoo
Primary Examiner
Art Unit 1723